PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

BIRD, William, E.
Bird Goën & Co.
Klein Dalenstraat 42A
B-3020 Winksele
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NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(PCT Rule 71.1)

Date of mailing *(day/month/year)*	23.05.2006
Applicant's or agent's file reference: K3234-PCT	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/BE2005/000032	04.03.2005	04.03.2004

Applicant
K.U. LEUVEN RESEARCH & DEVELOPMENT et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary report on patentability and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Bonomelli, F Tel. +49 89 2399-8459

Form PCT/IPEA/416 (January 2004)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference K3234-PCT	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/BE2005/000032	International filing date *(day/month/year)* 04.03.2005	Priority date *(day/month/year)* 04.03.2004
International Patent Classification (IPC) or national classification and IPC INV. C07H19/00 C07H19/06 C07H19/16 A61K31/706		
Applicant K.U. LEUVEN RESEARCH & DEVELOPMENT et al.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 8 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 14 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☒	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
30.09.2005	23.05.2006
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Klein, D Telephone No. +49 89 2399-7896

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/BE2005/000032

Box No. I Basis of the report

1. With regard to the **language**, this report is based on

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3(a) and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4(a))
   - ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-104	as originally filed

Claims, Numbers

1-7	received on 20.03.2006 with letter of 20.03.2006
8-14	received on 10.04.2006 with letter of 06.04.2006

Drawings, Sheets

1/15-15/15	as originally filed

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. II Priority

1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:
   - ☐ copy of the earlier application whose priority has been claimed (Rule 66.7(a)).
   - ☐ translation of the earlier application whose priority has been claimed (Rule 66.7(b)).

2. ☐ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rule 64.1). Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

   see separate sheet

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 12

because:

☒ the said international application, or the said claims Nos. 12 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*.

☐ no international search report has been established for the said claims Nos.

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b) and 13*ter*.2.

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-11,13-14
	No:	Claims	---
Inventive step (IS)	Yes:	Claims	1-11,14
	No:	Claims	13
Industrial applicability (IA)	Yes:	Claims	1-11,13-14
	No:	Claims	--

2. Citations and explanations (Rule 70.7):

see separate sheet

Reference is made to the following documents:

D1: WU, TONGFEI ET AL: "Deoxythreosyl phosphonate nucleosides as selective anti-HIV agents" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY , 127(14), 5056-5065 CODEN: JACSAT; ISSN: 0002-7863, 2005, XP002339526

D2: MCNULTY, JAMES ET AL: "On the direct 2,3-hydroxyl-group differentiation of tartaric acid esters" TETRAHEDRON LETTERS , 43(21), 3857 -3861 CODEN: TELEAY; ISSN: 0040-4039, 2002, XP002339527

D3: DUJARDIN, GILLES ET AL: "Asymmetric endoselective [4+2] heterocycloadditions of styrene dienophiles with chiral benzylidenepyruvic esters. Total synthesis of (-)-O-dimethylsugiresinol" TETRAHEDRON LETTERS , 38(9), 1555 -1558 CODEN: TELEAY; ISSN: 0040-4039, 1997, XP002339528

D4: GRIENGL, HERFRIED ET AL: "Phosphonoformate and phosphonoacetate derivatives of 5-substituted 2'-deoxyuridines: synthesis and antiviral activity" JOURNAL OF MEDICINAL CHEMISTRY , 31(9), 1831-9 CODEN: JMCMAR; ISSN: 0022-2623, 1988, XP002036743

D5: LAMBERT R W ET AL: "SYNTHSIS AND ANTIVIRAL ACTIVITY OF PHOSPHONOACETIC AND PHOSPHONOFORMIC ACID ESTERS OF 5-BROMO-2'-DEOXYURIDINE AND RELATED PYRIMIDINE NUCLEOSIDES AND ACYCLONUCLEOSIDES" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, vol. 32, no. 2, January 1989 (1989-01), pages 367-374, XP002911756 ISSN: 0022-2623

D6: KIM C U ET AL: "REGIOSPECIFIC AND HIGHLY STEREOSELECTIVE ELECTROPHILIC ADDITION TO FURANOID GLYCALS SYNTHESIS OF PHOSPHONATE NUCLEOTIDE ANALOGUES WITH POTENT ACTIVITY AGAINST HIV" JOURNAL OF ORGANIC CHEMISTRY, AMERICAN CHEMICAL SOCIETY. EASTON, US, vol. 56, no. 8, 1991, pages 2642-2647, XP002301628 ISSN: 0022-3263

Re Item II
Priority

D1 which is an intermediate document is not prior art according to the Chap II PCT proceedings.
Nevertheless, the extensive examination of that document, on the question whether it constitutes prior art or not, will depend essentially on the analysis of the claimed priority rights of the present application and will only be performed in the regional European proceedings to come.

As a remark, it seems that the claimed subject-matter is not fully supported by the priority document, as many more compounds are claimed in the application than disclosed in the priority document.

Re Item III
Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

For the assessment of the present claim 12 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

For this reason no opinion will be given concerning claim 11.

Re Item V
Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Novelty (Art. 33(2) PCT) :

Claims 1-11,13-14 appear to be new in the light of the cited prior art.

Inventive step (Art. 33(3) PCT) :

a) D4, which is considered to represent the closest prior art, discloses antiviral compounds bearing a 5'-hydroxymethyl group and either a 4'-phosphono or a 4'-phosphonomethylcarbonyl group from which the subject-matter of the present application differs by these two functional features (4' and 5' modifications).

Since none of the available prior art suggest the combination of these two modifications/adaptations, the subject-matter of claims 1-11,14 is considered inventive.

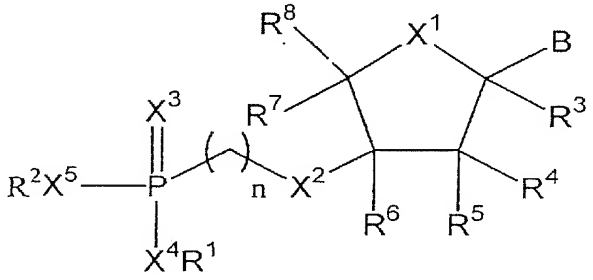
b) For an intermediate to be considered inventive, this compound must share essential technical feature(s) with the final compound(s) (i.e. a protected "final" compound). In the present case, it is clear that the 4'-phosphonoalkyl derivative constitutes this essential technical feature. However, derivatives of claim 13 do not possess this feature. Therefore they cannot be considered inventive.

Industrial application (Art. 33(4) PCT):

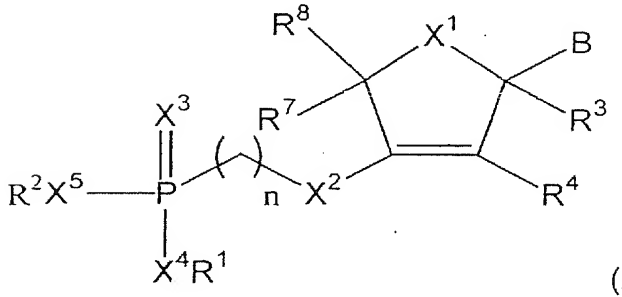
Claims 1-11,13-14 comply with the requirements of Art. 33(4) PCT.

CLAIMS

1. A compound including a heterocyclic nucleobase attached to a first carbon atom of an optionally substituted five-member saturated or mono-unsaturated heterocyclic group selected from tetrahydrofuranyl, tetrahydrothienyl, dihydrofuranyl and dihydrothienyl and further including a phosphonoalkoxy or phosphonothioalkyl group attached to a second carbon atom of said five-member saturated or mono-unsturated heterocyclic group, said first carbon atom being adjacent to the heteroatom of said five-member saturated or mono-unsturated heterocyclic group, and said second carbon atom being adjacent neither to the heteroatom nor to the first carbon atom of said five-member saturated or mono-unsturated heterocyclic group, said compound being represented by one of the general formulae (II) and (XIX):



(II), and



(XIX)

wherein:

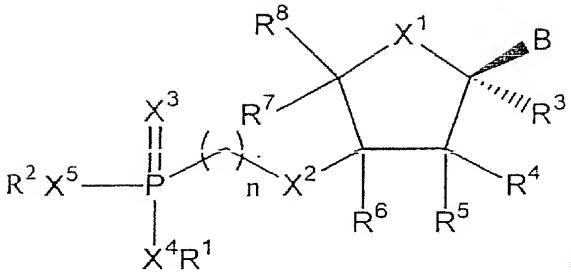
- X^1, X^2, X^3, X^4 and X^5 are each each independently selected from the group consisting of oxygen and sulfur,
- B is a natural or non-natural heterocyclic nucleobase,

- R^1 and R^2 are each independently selected from the group consisting of hydrogen; $(-PO_3R^{16})_m-PO_3R^{17}R^{18}$; alkyl; alkenyl; alkynyl; cycloalkyl; cycloalkenyl; cycloalkynyl; aryl; arylalkyl; heterocyclic; heterocyclic-alkyl; acyloxyalkyl; acyloxyalkenyl; acyloxyalkynyl; acyloxyaryl; acyloxyarylalkyl; acyloxyarylalkenyl; acyloxyarylalkynyl; dialkylcarbonate; alkylarylcarbonate; alkylalkenylcarbonate; alkylalkynylcarbonate; alkenylarylcarbonate; alkynyl-arylcarbonate; alkenylalkynylcarbonate; dialkenylcarbonate; dialkynyl-carbonate; wherein said alkyl, alkenyl and alkynyl optionally contains one or more heteroatoms in or at the end of the hydrocarbon chain, said heteroatoms being independently selected from the group consisting of oxygen, sulfur and nitrogen;
- R^3, R^4, R^5, R^6, R^7 and R^8 are each independently selected from the group consisting of hydrogen, azido, halogen, cyano, alkyl, alkenyl, alkynyl, SR^{14} and OR^{14};
- R^{14} is selected from hydrogen; alkyl; alkenyl; alkynyl; cycloalkyl; cycloalkenyl; cycloalkynyl; aryl; heterocyclic; arylalkyl; heterocyclic-alkyl; acyloxyalkyl; wherein said alkyl, alkenyl and alkynyl optionally contain one or more heteroatoms in or at the end of the hydrocarbon chain, said heteroatoms being independently selected from the group consisting of oxygen, sulfur and nitrogen;
- R^{16}, R^{17} and R^{18} are independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; cycloalkyl; cycloalkenyl; cycloalkynyl; aryl; arylalkyl; heterocyclic ring; heterocyclic ring-alkyl; acyloxyalkyl; wherein said alkyl, alkenyl and alkynyl optionally contain one or more heteroatoms in or at the end of the hydrocarbon chain, said heteroatoms being independently selected from the group consisting of oxygen, sulfur and nitrogen;
- X^4 and R^1, or X^5 and R^2 may together form an amino-acid residue or polypeptide wherein a carboxyl function of said amino-acid residue being at a distance from the amidate nitrogen not further than 5 atoms is esterified;

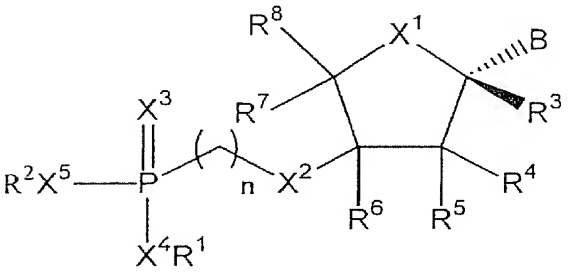
- X^4 and R^1 or X^5 and R^2 may together form a group having the formula – $OC(R^9)_2OC(O)Y(R^{10})_a$ wherein Y = N or O, a = 1 when Y is O and a = 1 or 2 when Y is N;
- R^9 is selected from the group consisting of hydrogen, alkyl, aryl, alkenyl, alkynyl, alkenylaryl, alkynylaryl or alkylaryl, wherein each of said alkyl, alkenyl, alkynyl and aryl groups is optionally substituted with one or more atoms or groups selected from the group consisting of halo, cyano, azido, nitro and OR^{14};
- R^{10} is selected from the group consisting of hydrogen, alkyl, aryl, alkenyl, alkynyl, alkenylaryl, alkynylaryl and alkylaryl, wherein each of said alkyl, alkenyl, alkynyl and aryl groups is optionally substituted with one or more atoms or groups selected from the group consisting of halo, cyano, azido, nitro, OR^{14} and $NR^{11}R^{12}$;
- R^{11} and R^{12} are each independently selected from the group consisting of hydrogen and alkyl, provided that at least one of R^{11} and R^{12} is not hydrogen;
- n is an integer representing the number of methylene groups between X_2 and P, each of said methylene groups being optionally and independently substituted with one or two substituents selected from the group consisting of halogen, hydroxyl, sulhydryl and C_{1-4} alkyl, and n being selected from 1, 2, 3, 4, 5 and 6; and
- m is 0 or 1,

including pharmaceutically acceptable salts, solvates, stereoisomers and prodrugs thereof.

2. A compound according to claim 1, being represented by one of the general formulae (III) to (XVIII):



(III),



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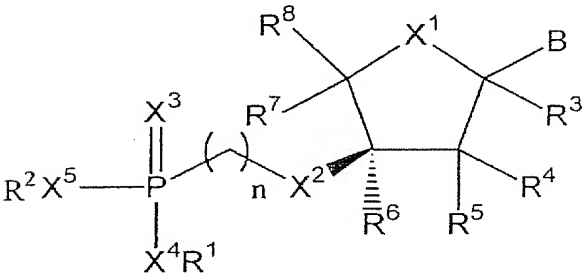

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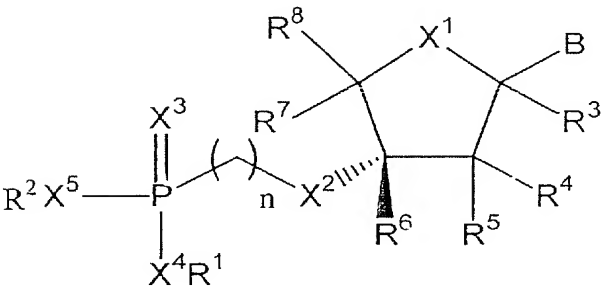

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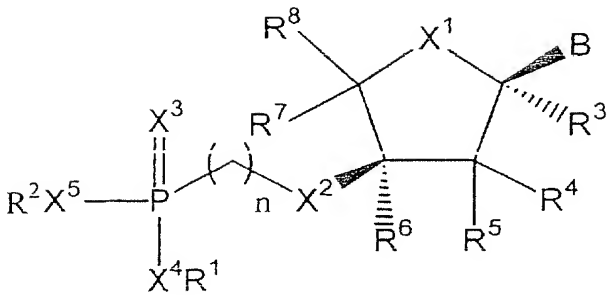

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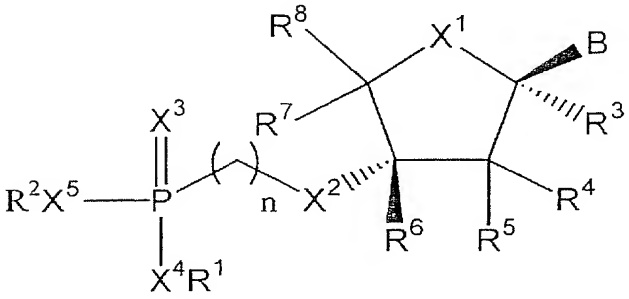

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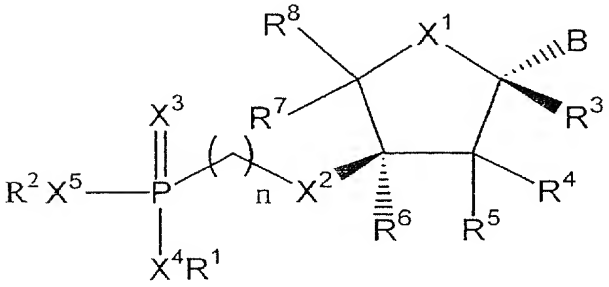

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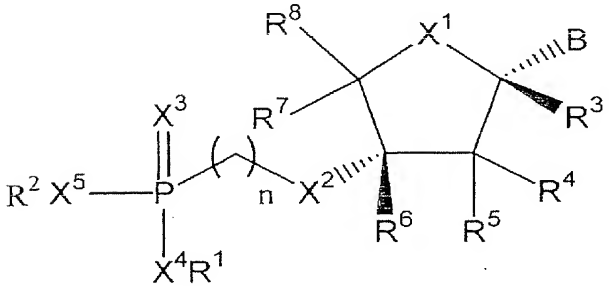

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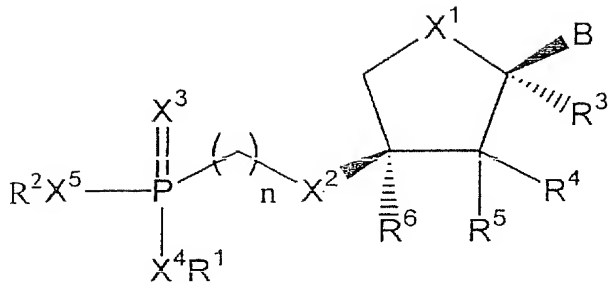
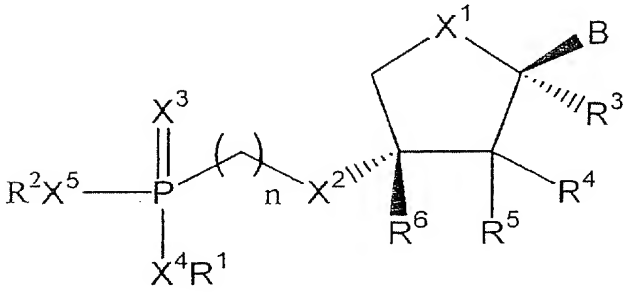


(XI),



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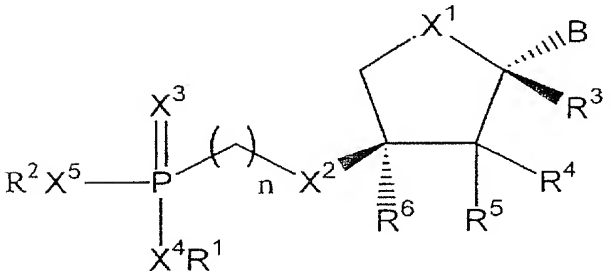
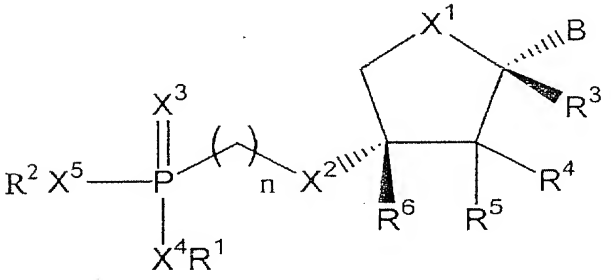


(XIII)



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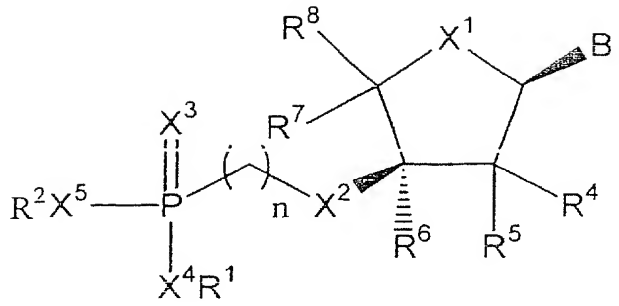
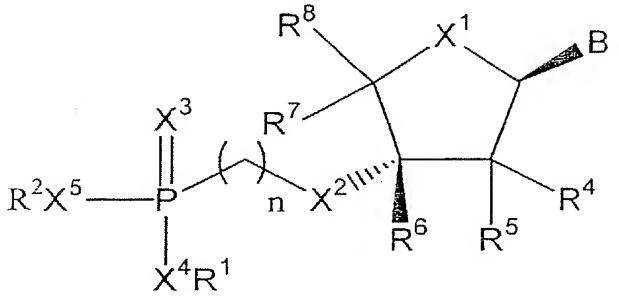
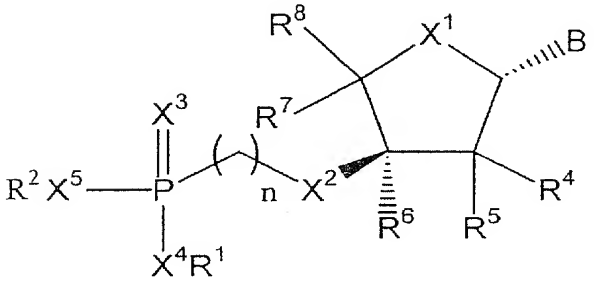


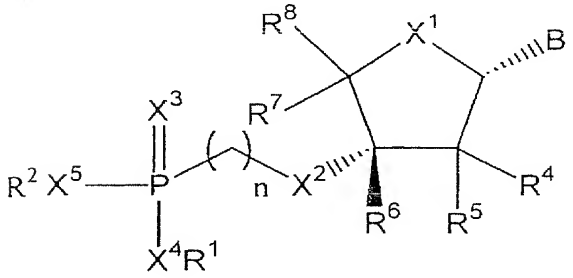
(XV),



(XVI)



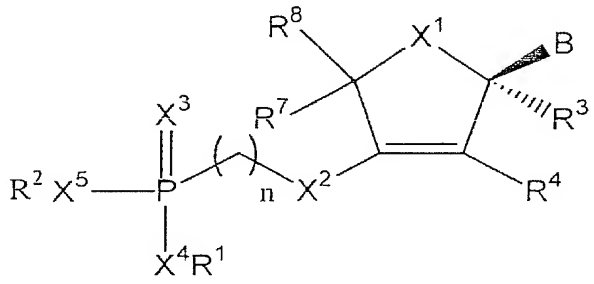
(XVII), and



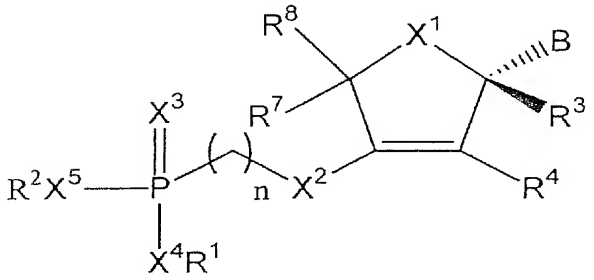
(XVIII)

wherein n, m, B, X^1, X^2, X^3, X^4, X^5, R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11}, R^{12}, R^{14}, R^{16}, R^{17} and R^{18} are defined as in formula (II), including pharmaceutically acceptable salts, solvates, stereoisomers and prodrugs thereof.

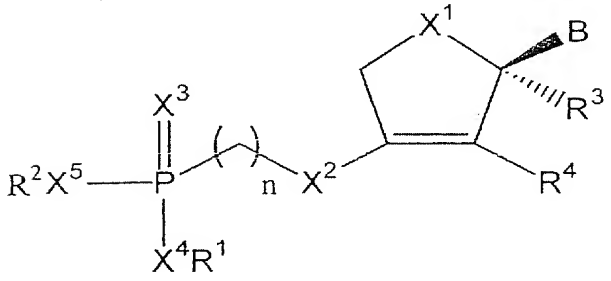
3. A compound according to claim 1, being represented by any of the following formulae (XX) to (XXVI):



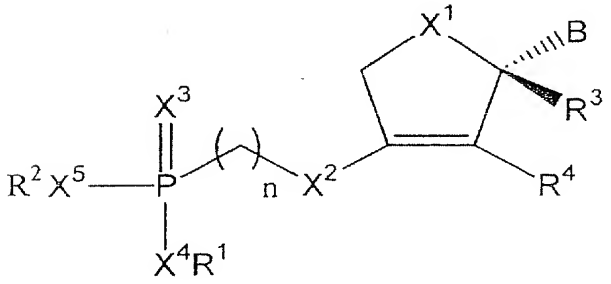
(XX),



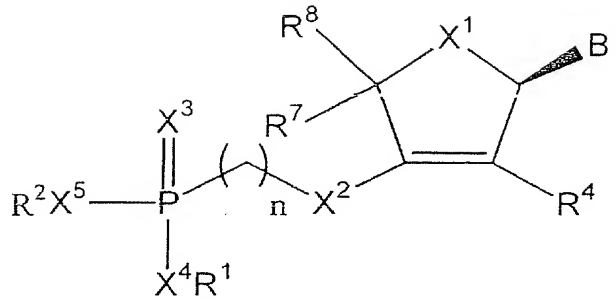
(XXI),



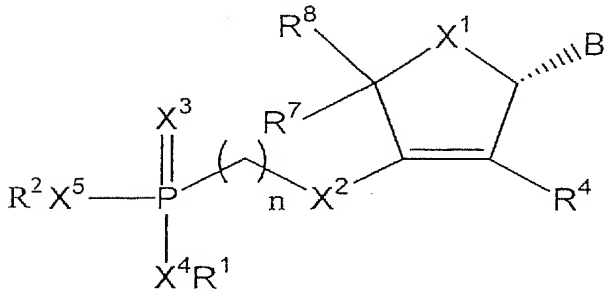
(XXII),



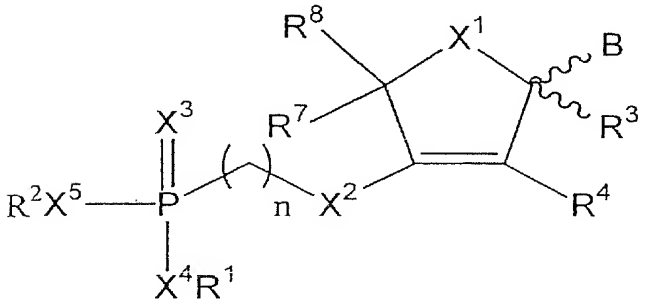
(XXIII),



(XXIV),



(XXV), and



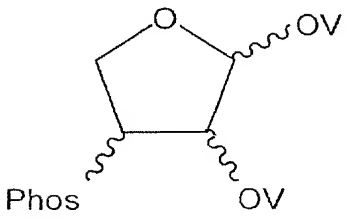
(XXVI),

wherein n, m, B, X^1, X^2, X^3, X^4, X^5, R^1, R^2, R^3, R^4, R^7, R^8, R^9, R^{10}, R^{11}, R^{12}, R^{14}, R^{16}, R^{17} and R^{18} are defined as in formula (II), including pharmaceutically acceptable salts, solvates, stereoisomers and prodrugs thereof.

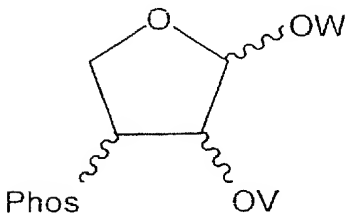
4. A compound according to any of claims 1 to 3, wherein B is selected from the group consisting of hypoxanthine, guanine, adenine, cytosine, inosine, thymine, uracil, xanthine, 8-aza derivatives of 2-aminopurine, 2,6-diaminopurine, 2-amino-6-chloropurine, hypoxanthine, inosine and xanthine;

7-deaza-8-aza derivatives of adenine, guanine, 2-aminopurine, 2,6-diaminopurine, 2-amino-6-chloropurine, hypoxanthine, inosine and xanthine; 1-deaza derivatives of 2-aminopurine, 2,6-diaminopurine, 2-amino-6-chloropurine, hypoxanthine, inosine and xanthine; 7-deaza derivatives of 2-aminopurine, 2,6-diaminopurine, 2-amino-6-chloropurine, hypoxanthine, inosine and xanthine; 3-deaza derivatives of 2-aminopurine, 2,6-diaminopurine, 2-amino-6-chloropurine, hypoxanthine, inosine and xanthine; 6-azacytosine; 5-fluorocytosine; 5-chlorocytosine; 5-iodocytosine; 5-bromocytosine; 5-methylcytosine; 5-bromovinyluracil; 5-fluorouracil; 5-chlorouracil; 5-iodouracil; 5-bromouracil; 5-trifluoromethyluracil; 5-methoxymethyluracil; 5-ethynyluracil and 5-propynyluracil.

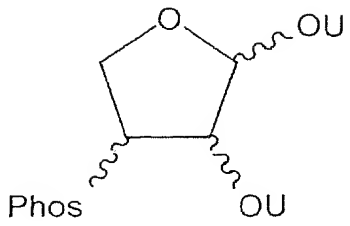
5. A compound represented by one of the following general formulae (XXXI) to (XXXVI):



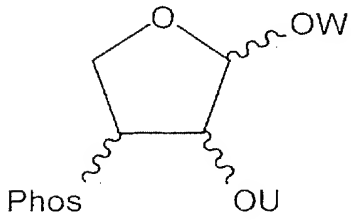
(XXXI),



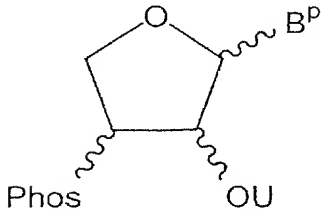
(XXXII),



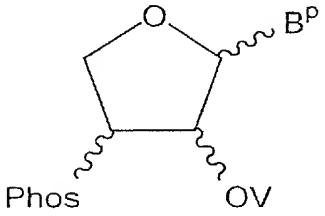
(XXXIII),



(XXXIV),



(XXXV), and



(XXXVI),

wherein:

- U is an acyl group,
- V is a silyl group,
- W is an alkyl group,
- the snake-like symbol means any stereochemical arrangement of the respective bond,
- B^p is an optionally protected heterocyclic nucleobase, and
- Phos is an O-protected phosphonoalkoxy group or phosphonothioalkyl group.

6. Use of a compound according to claim 5 as an intermediate for making a compound according to any of claims 1 to 4.

7. A compound according to any of claims 1 to 4, being selected from the group consisting of :

1-(N^6-benzoyladenin-9-yl)-2-O-benzoyl-3-O-(diisopropylphosphonomethyl)-L-threose (**11**);

1-(thymin-1-yl)-2-O-benzoyl-3-O-(diisopropylphosphonomethyl)-L-threose(**12**);

1-(uracil-1-yl)-2-O-benzoyl-3-O-(diisopropylphosphonomethyl)-L-threose (**13**);

1-(N^4-acetylcytosin-1-yl)-2-O-benzoyl-3-O-(diisopropylphosphonomethyl)-L-threose (**14**);

1-(adenin-9-yl)-3-O-(diisopropylphosphonomethyl)-L-threose (**15**);

1-(thymin-1-yl)-3-O-(diisopropylphosphonomethyl)-L-threose (**16**);

1-(uracil-1-yl)-3-O-(diisopropylphosphonomethyl)-L-threose (**17**);

1-(cytosin-1-yl)-3-O-(diisopropylphosphonomethyl)-L-threose (**18**);

1-(adenin-9-yl)-2-deoxy-3-O-(diisopropylphosphonomethyl)-L-threose (**19**);

1-(thymin-1-yl)-2-deoxy-3-O-(diisopropylphosphonomethyl)-L-threose (**20**);

1-(uracil-1-yl)-2-deoxy-3-O-(diisopropylphosphonomethyl)-L-threose (**21**);

1-(cytosin-1-yl)-2-deoxy-3-O-(diisopropylphosphonomethyl)-L-threose (**22**);

1-(adenin-9-yl)-3-O-(phosphonomethyl)-L-threose sodium salt (**3a**);

1-(thymin-1-yl)-3-O-(phosphonomethyl)-L-threose sodium salt (**3b**);

1-(uracil-1-yl)-3-O-(phosphonomethyl)-L-threose sodium salt (**3c**);

1-(cytosin-1-yl)-3-O-(phosphonomethyl)-L-threose sodium salt (**3d**);

1-(adenin-1-yl)-2-deoxy-3-O-(phosphonomethyl)-L-threose sodium salt (**3e**);

1-(thymin-1-yl)-2-deoxy-3-O-(phosphonomethyl)-L-threose sodium salt (**3f**);

1-(uracil-1-yl)-2-deoxy-3-O-(phosphonomethyl)-L-threose sodium salt (**3g**);

1-(cytidin-1-yl)-2-deoxy-3-O-(phosphonomethyl)-L-threose sodium salt (**3h**);

a pharmaceutically acceptable salt , an stereoisomer, a solvate or a pro-drug thereof.

7. The use of a compound according to any of the claims 1 to 4, for the manufacture of a medicament for the prevention or treatment of a viral infection in a mammal.

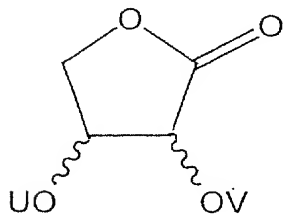
8. The use according to claim 7, wherein said viral infection is an infection by the Human Immunodeficiency Virus (HIV).

9. A pharmaceutical composition comprising a compound according to any of the claims 1 to 4 as an active ingredient in admixture with at least a pharmaceutically acceptable carrier.

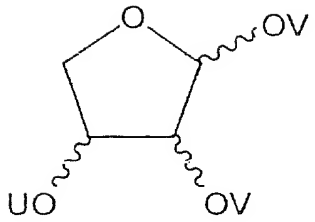
10. A pharmaceutical composition according to claim 9, further comprising an antiviral agent.

11. A method of treatment or prevention of a viral infection in a mammal, comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound according to any of claims 1 to 4.

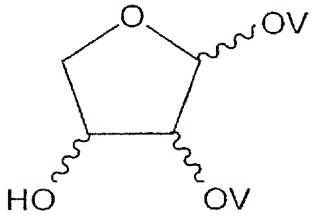
12. A compound represented by one of the following general formulae (XXVIII) to (XXX):



(XXVIII),



(XXIX), and



(XXX),

wherein:

- U is an acyl group,
- V is a silyl group, and
- the snake-like symbol means any stereochemical arrangement of the respective bond.

13. Use of a compound according to claim 12 as an intermediate for making a compound according to any of claims 1 to 4.